

IN THE CLAIMS:

✓
Please cancel claims 1-8 without prejudice to revival for subsequent prosecution. Please add new claims 24 and 25.

24. (new) A barley plant made by the method of claim 9.

25. (new) A population of barley plants made by the method of claim 9.

REMARKS

With entry of the current amendment, claims 1-8 have been cancelled and new claims 24 and 25 have been added. Claims 17-23 are withdrawn from consideration. Thus, claims 9-16, 24, and 25 are under examination. For convenience, a copy of the claims currently under examination is attached.

The rejections are addressed in the order set out in the Office Action mailed June 3, 2002.

Rejection under 35 U.S.C. § 112, first paragraph--written description

Claims 1-8 were rejected as allegedly lacking adequate written description. The rejection is obviated by the cancellation of the claims.

Rejection under 35 U.S.C. § 103

Claims 1-16 stand rejected as allegedly obvious over McElroy *et al.* in view of Wan *et al.* and Bancroft *et al.* (claims 1-14), and further in view of Perera *et al.* (Claims 15 and 16). The rejection alleges that the success of Wan *et al.* in transforming barley, the success of McElroy *et al.* in demonstrating Ac transposase-mediated excision of *Ds* in barley cells, and the successful use of *AcDs* transposition in other plants, *e.g.*, *Arabidopsis*, would have motivated one of skill in the art to combine these teachings with a reasonable expectation of success. In particular, the Examiner argues that

demonstration of *Ac*-transposase-mediated excision of *Ds* in barley cells would indicate that the *Ac/Ds* system could be used in barley to generate stable transformants.

The rejection as applied to claims 1-8 is moot in view of the cancellation of those claims; with respect to claims 9-16, Applicants respectfully traverse. As maintained in Applicants' previous responses, the Examiner has not established a proper case of *prima facie* obviousness. A *prima facie* case of obviousness requires that the prior art suggest all of the elements of the claimed invention, that there is a motivation to combine the reference teachings, and that there is a reasonable expectation of success at arriving at the claimed invention. Applicants submit that at the time of the invention, one of skill in the art had no motivation to use the *Ac/Ds* system in barley due to factors known to those in the art, *e.g.*, the methylation status of the barley genome. Moreover, even if one were to try to use the system in barley, there was no reasonable expectation of success. As further evidence that the combination of references does not render the invention obvious, Applicants submit herewith a Declaration pursuant to 37 C.F.R. § 1.132 by Peggy Lemaux, Ph.D, which provides objective reasons as to why one of skill could not reasonably expect that the *Ac/Ds* system would provide a stable transformation system in barley.

In the Declaration, Dr. Lemaux explains that because of certain characteristics of the barley cell and genome, in particular, the amount of methylation and gene silencing, it could not reasonably be expected that the *Ac/Ds* system could generate stable transformants, *i.e.*, transformants in which the transposable element can be reactivated and reinsert into the genome. Specifically, she notes that methylation can lead to instability and loss of a sequence from the genome, and that such phenomena were frequently observed in barley (paragraph 8 of the Declaration). She further explains that those in the art believe that foreign sequences can be readily distinguished from the highly GC-rich barley genome and preferentially inactivated. This can result not only in the instability of foreign sequences, but also gene silencing (paragraph 9). Gene silencing can lead to lack of activity of the encoded protein or compromise the ability of an introduced sequence to perform its function. Thus, methylation may silence

expression of a gene, for example an *Ac* transposase gene or a transposition cassette associated with a *Ds* element. Further, methylation can lead to direct inactivation of transposition, for example, by preventing a *Ds* element from stably integrating and retaining the ability to reinsert into another region of the genome in the presence of transposase activity. Lastly, it is also believed that the inverted repeats in the *Ds* elements needed for recognition by *Ac* transposases and transposition, can trigger methylation-induced silencing that prevents re-activation of *Ds*.

In order for the *Ac/Ds* system to provide stable transformants in barley, the elements must be introduced into plants and stably integrate into the genome (that is, they must not be subject to rearrangement, deletions, etc. over time). Further, they must retain their ability to transpose, *i.e.*, the transposase must not be silenced and the recognition sites must not be methylated or changed in sequences. Lastly, the *Ds* elements must retain the ability to re-insert into the genome. However, as explained by Dr. Lemaux, the barley genome is highly methylated and methylation of foreign sequences in barley was known to frequently lead to instability and/or gene silencing. How then, could one of skill predict that methylation would not lead to inactivation of the *Ac/Ds* system?

Dr. Lemaux concludes that at the time of the invention, there was no reason to expect that the *Ac/Ds* system would be capable of generating stable barley transformations. In particular, she believes that there was no reason to expect that a *Ds* element would be able to re-integrate into the highly methylated barley genome or would not itself become methylated and incapable of excising or re-integrating in a stably transformed barley cells.

Thus, the combination of references cited by the Examiner at best only provides a motivation to try to use the *Ac/Ds* system in barley to generate stable transformants. However, there was no reasonable expectation that it would be successful. Accordingly, the invention is unobvious over the cited art. Applicants therefore respectfully request withdrawal of the rejection.

Lemaux, *et al.*
Application No.: 09/384,811
Page 5

PATENT

Rejection under 35 U.S.C. § 101

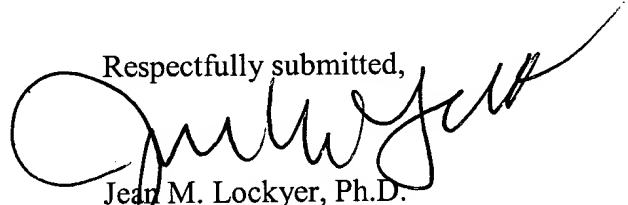
Claims 1-8 were rejected as allegedly lacking utility. The rejection is obviated by the cancellation of the claims.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



Jean M. Lockyer, Ph.D.
Reg. No. 44,879

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, 8th Floor
San Francisco, California 94111-3834
Tel: 415-576-0200
Fax: 415-576-0300
JML:jml
SF 1407448 v1